

10/630,344

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	964	(435/7.24).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:51
L2	248	(435/40.51).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:52
L3	1921	(436/63).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:53
L4	2224	(435/29).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:53
L5	4824	L1 OR L2 OR L3 OR L4	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L6	2000	ANGINA?	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L7	342	STENOCARDIA	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L8	6	CORONARISM	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L9	7	CARDIAGRA	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L10	2345	L6 OR L7 OR L8 OR L9	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L11	51078	INTERLEUKIN	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55

EAST Search History

L12	47077	INTERFERON	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L13	63027	CYTOKINE	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L14	13903	LYMPHOKINE	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:56
L15	98453	L11 OR L12 OR L13 OR L14	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:56
L16	3	L5 AND L10 AND L15	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:56

10/630,344

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USPAT2
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NEWS 5 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
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NEWS 14 FEB 28 TOXCENTER reloaded with enhancements
NEWS 15 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral
property data
NEWS 16 MAR 01 INSPEC reloaded and enhanced
NEWS 17 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18 MAR 08 X.25 communication option no longer available after June 2006
NEWS 19 MAR 22 EMBASE is now updated on a daily basis
NEWS 20 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC
thesaurus added in PCTFULL
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NEWS 23 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24 APR 12 Improved structure highlighting in FQHIT and QHIT display
in MARPAT
NEWS 25 APR 12 Derwent World Patents Index to be reloaded and enhanced during
second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
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FILE 'HOME' ENTERED AT 12:06:48 ON 24 APR 2006

=> FILE MEDLINE

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'MEDLINE' ENTERED AT 12:07:02 ON 24 APR 2006

FILE LAST UPDATED: 22 APR 2006 (20060422/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

<http://www.nlm.nih.gov/mesh/>

http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S ANGINA?

L1 48229 ANGINA?

=> S STENOCARDIA

828 STENOCARDIA

20 STENOCARDIAS

L2 847 STENOCARDIA

(STENOCARDIA OR STENOCARDIAS)

=> S CORONARISM

0 CORONARISM

L3 0 CORONARISM

=> S CARDIAGRA

0 CARDIAGRA

L4 0 CARDIAGRA

=> S L1 OR L2

L5 48317 L1 OR L2

=> S INTERLEUKIN

144796 INTERLEUKIN

7421 INTERLEUKINS

L6 147358 INTERLEUKIN

(INTERLEUKIN OR INTERLEUKINS)

=> S INTERFERON

92119 INTERFERON

19791 INTERFERONS

L7 97261 INTERFERON

(INTERFERON OR INTERFERONS)

=> S CYTOKINE

75299 CYTOKINE

96297 CYTOKINES

L8 132678 CYTOKINE

(CYTOKINE OR CYTOKINES)

=> S LYMPHOKINE

9068 LYMPHOKINE

18810 LYMPHOKINES

L9 25166 LYMPHOKINE

(LYMPHOKINE OR LYMPHOKINES)

=> S L6 OR L7 OR L8 OR L9

L10 288379 L6 OR L7 OR L8 OR L9

=> T(W) (CELL OR LYMPHOCYTE)

T(W) (CELL IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

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=> S T(W) (CELL OR LYMPHOCYTE)

4176845 T

2000119 CELL

1807454 CELLS

2663835 CELL

(CELL OR CELLS)

195552 LYMPHOCYTE

331266 LYMPHOCYTES

390516 LYMPHOCYTE

(LYMPHOCYTE OR LYMPHOCYTES)

L11 257834 T(W) (CELL OR LYMPHOCYTE)

=> S L5 AND L10 AND L11

L12 57 L5 AND L10 AND L11

=> S L12 NOT 2001-2006/PY

3043636 2001-2006/PY

(20010000-20069999/PY)

L13 13 L12 NOT 2001-2006/PY

=> SAVE TEMP

ENTER L#, L# RANGE, ALL, OR (END):L13

ENTER NAME OR (END):ANGINA/A

ANSWER SET L13 HAS BEEN SAVED AS 'ANGINA/A'

=> D L13 1-13 BIB AB

L13 ANSWER 1 OF 13 MEDLINE on STN

AN 2000329934 MEDLINE

DN PubMed ID: 10869258

TI Monoclonal T-cell proliferation and plaque instability
in acute coronary syndromes.

AU Liuzzo G; Goronzy J J; Yang H; Kopecky S L; Holmes D R; Frye R L; Weyand C
M

CS Department of Medicine, Division of Rheumatology, Mayo Clinic and
Foundation, Rochester, MN 55905, USA.

NC R01-AR41974 (NIAMS)

R01-AR42527 (NIAMS)

R01EY11916 (NEI)

SO Circulation, (2000 Jun 27) Vol. 101, No. 25, pp. 2883-8.

Journal code: 0147763. E-ISSN: 1524-4539.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 200007
 ED Entered STN: 28 Jul 2000
 Last Updated on STN: 21 May 2001
 Entered Medline: 19 Jul 2000
 AB BACKGROUND: Unstable **angina** (UA) is associated with systemic inflammation and with expansion of **interferon-gamma-producing T lymphocytes**. The cause of T-cell activation and the precise role of activated T cells in plaque instability are not understood. METHODS AND RESULTS: Peripheral blood T cells from 34 patients with stable **angina** and 34 patients with UA were compared for the distribution of functional T-cell subsets by flow cytometric analysis. Clonality within the T-cell compartment was identified by T-cell receptor spectrotyping and subsequent sequencing. Tissue-infiltrating T cells were examined in extracts from coronary arteries containing stable or unstable plaque. The subset of CD4(+)CD28(null) T cells was expanded in patients with UA and infrequent in patients with stable **angina** (median frequencies: 10.8% versus 1.5%, P<0.001). CD4(+)CD28(null) T cells included a large monoclonal population, with 59 clonotypes isolated from 20 UA patients. T-cell clonotypes from different UA patients used antigen receptors with similar sequences. T-cell receptor sequences derived from monoclonal T-cell populations were detected in the culprit but not in the nonculprit lesion of a patient with fatal myocardial infarction. CONCLUSIONS: UA is associated with the emergence of monoclonal T-cell populations, analogous to monoclonal gammopathy of unknown significance. Shared T-cell receptor sequences in clonotypes of different patients implicate chronic stimulation by a common antigen, for example, persistent infection. The unstable plaque but not the stable plaque is invaded by clonally expanded T cells, suggesting a direct involvement of these lymphocytes in plaque disruption.

L13 ANSWER 2 OF 13 MEDLINE on STN
 AN 2000288058 MEDLINE
 DN PubMed ID: 10829249
 TI Inflammation and acute coronary syndromes.
 AU Biasucci L M; Liuzzo G; Angiolillo D J; Sperti G; Maseri A
 CS Institute of Cardiology, Catholic University, Rome, Italy..
 biasucci@pelagus.it
 SO Herz, (2000 Mar) Vol. 25, No. 2, pp. 108-12. Ref: 46
 Journal code: 7801231. ISSN: 0340-9937.
 CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LA English
 FS Priority Journals
 EM 200006
 ED Entered STN: 6 Jul 2000
 Last Updated on STN: 6 Jul 2000
 Entered Medline: 23 Jun 2000
 AB The presence of inflammatory infiltrates in unstable coronary plaques suggests that inflammatory processes may contribute to the pathogenesis of these syndromes. In patients with unstable **angina**, coronary atherosclerotic plaques are characterized by the presence of macrophages, and to a lesser extent, **T-lymphocytes**, at the immediate site of either plaque rupture or superficial erosion; moreover, the rupture-related inflammatory cells are activated, indicating ongoing inflammation at the site of plaque disruption. These observations are confirmed by clinical studies demonstrating activated circulating neutrophils, lymphocytes and monocytes, and increased concentrations of

pro-inflammatory cytokines, such as interleukin (IL) 1 and 6, and of acute phase reactants in patients with unstable angina and myocardial infarction. In particular elevated levels of C-reactive protein are associated with an increased risk of in-hospital and 1 to 2 years new coronary events in patients with unstable angina, but are also associated with an increased long-term risk of death and myocardial infarction in apparently normal subjects. Thus, accumulating evidence suggests that inflammation may cause local endothelial activation and, possibly, plaque fissure, leading to unstable angina and infarction. Although no information is yet available on the causes of inflammation and on its localization, these novel lines of research may open the way to a different approach to the patient with acute coronary syndromes.

L13 ANSWER 3 OF 13 MEDLINE on STN
 AN 2000225898 MEDLINE
 DN PubMed ID: 10762452
 TI Changing concepts of atherogenesis.
 AU Libby P
 CS Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA.. plibby@rics.bwh.harvard.edu
 NC HL34636 (NHLBI)
 SO Journal of internal medicine, (2000 Mar) Vol. 247, No. 3, pp. 349-58.
 Ref: 85
 Journal code: 8904841. ISSN: 0954-6820.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LA English
 FS Priority Journals
 EM 200005
 ED Entered STN: 25 May 2000
 Last Updated on STN: 25 May 2000
 Entered Medline: 12 May 2000
 AB This review discusses three stages in the life history of an atheroma: initiation, progression and complication. Recruitment of mononuclear leucocytes to the intima characterizes initiation of the atherosclerotic lesion. Specific adhesion molecules expressed on the surface of vascular endothelial cells mediate leucocyte adhesion: the selectins and members of the immunoglobulin superfamily such as vascular cell adhesion molecule-1 (VCAM-1). Once adherent, the leucocytes enter the artery wall directed by chemoattractant chemokines such as macrophage chemoattractant protein-1 (MCP-1). Modified lipoproteins contain oxidized phospholipids which can elicit expression of adhesion molecule and cytokines implicated in early atherogenesis. Progression of atheroma involves accumulation of smooth muscle cells which elaborate extracellular matrix macromolecules. These processes appear to result from an eventual net positive balance of growth stimulatory versus growth inhibitory stimuli, including proteins (cytokines and growth factors) and small molecules (e.g. prostanoids and nitric oxide). The clinically important complications of atheroma usually involve thrombosis. Arterial stenoses by themselves seldom cause acute unstable angina or acute myocardial infarction. Indeed, sizeable atheroma may remain silent for decades or produce only stable symptoms such as angina pectoris precipitated by increased demand. Recent research has furnished new insight into the molecular mechanisms that cause transition from the chronic to the acute phase of atherosclerosis. Thrombus formation usually occurs because of a physical disruption of atherosclerotic plaque. The majority of coronary thromboses result from a rupture of the plaque's protective fibrous cap, which permits contact between blood and the highly thrombogenic material located in the lesion's lipid core, e.g. tissue factor. Interstitial collagen accounts for most of the tensile strength of the plaque's fibrous cap. The amount of collagen in the lesion's fibrous cap depends upon its rate of biosynthesis stimulated by factors released from platelets (e.g. transforming growth factor beta or

platelet-derived growth factor), but inhibited by gamma interferon, a product of activated T cells found in plaques. Degradation by specialized enzymes (matrix metalloproteinases) also influences the level of collagen in the plaque's fibrous cap. Such studies illustrate how the application of cellular and molecular approaches has fostered a deeper understanding of the pathogenesis of atherosclerosis. This increased knowledge of the basic mechanisms enables us to understand how current therapies for atherosclerosis may act. Moreover, the insights derived from recent scientific advances should aid the discovery of new therapeutic targets that would stimulate development of novel treatments. Such new treatments could further reduce the considerable burden of morbidity and mortality due to this modern scourge, and reduce reliance on costly technologies that address the symptoms rather than the cause of atherosclerosis.

L13 ANSWER 4 OF 13 MEDLINE on STN
 AN 2000040177 MEDLINE
 DN PubMed ID: 10571971
 TI Perturbation of the T-cell repertoire in patients with unstable angina.
 AU Liuzzo G; Kopecky S L; Frye R L; O'Fallon W M; Maseri A; Goronzy J J; Weyand C M
 CS Department of Medicine, Mayo Clinic, Rochester, MN 55905, USA.
 SO Circulation, (1999 Nov 23) Vol. 100, No. 21, pp. 2135-9.
 Journal code: 0147763. E-ISSN: 1524-4539.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199912
 ED Entered STN: 13 Jan 2000
 Last Updated on STN: 21 May 2001
 Entered Medline: 9 Dec 1999
 AB BACKGROUND: Monocytes are constitutively activated in unstable angina (UA), resulting in the production of IL-6 and the upregulation of acute phase proteins. Underlying mechanisms are not understood. To explore whether the production of the potent monocyte activator IFN-gamma is altered in UA, we compared cytokine production by T lymphocytes in patients with UA (Braunwald's class IIIB) and with stable angina (SA). METHODS AND RESULTS: Peripheral blood lymphocytes were collected at the time of hospitalization and after 2 and 12 weeks. Cytokine-producing CD4(+) and CD8(+) T cells were quantified by 3-color flow cytometry after stimulation with phorbol myristate acetate and ionomycin. UA was associated with an increased number of CD4(+) and CD8(+) T cells producing IFN-gamma, whereas patients with SA had higher frequencies of IL-2(+) and IL-4(+) CD4(+) T cells. Expansion of the IFN-gamma(+) T-cell population in UA persisted for at least 3 months. Increased production of IFN-gamma in UA could be attributed to the expansion of an unusual subset of T cells, CD4(+)CD28(null) T cells. CONCLUSIONS: Patients with UA are characterized by a perturbation of the functional T-cell repertoire with a bias toward IFN-gamma production, suggesting that monocyte activation and acute phase responses are consequences of T-cell activation. IFN-gamma is produced by CD4(+)CD28(null) T cells, which are expanded in UA and distinctly low in SA and controls. The emergence of CD4(+)CD28(null) T cells may result from persistent antigenic stimulation.

L13 ANSWER 5 OF 13 MEDLINE on STN
 AN 2000017427 MEDLINE
 DN PubMed ID: 10551265
 TI Activation of monocytes, T-lymphocytes and plasma inflammatory markers in angina patients.

*Post dates
provisional*

AU Lee W H; Lee Y; Kim J R; Chu J A; Lee S Y; Jung J O; Kim J S; Kim S; Seo J
 D; Rhee S S; Park J E
 CS Clinical Research Center, Samsung Biomedical Research Institute, Seoul,
 Korea.
 SO Experimental & molecular medicine, (1999 Sep 30) Vol. 31, No. 3, pp.
 159-64.
 Journal code: 9607880. ISSN: 1226-3613.
 CY KOREA (SOUTH)
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199911
 ED Entered STN: 11 Jan 2000
 Last Updated on STN: 11 Jan 2000
 Entered Medline: 23 Nov 1999
 AB Inflammation and activation of immune cells have important roles in the
 pathogenesis of atherosclerosis. We analyzed the plasma levels of
 inflammatory markers and the degree of activation of peripheral blood
 monocytes and T-lymphocytes isolated from 12 unstable
 angina, 12 stable angina, and 12 normal subjects. In
 20%-33% of patients, monocytes expressed high basal levels of IL-8, tissue
 factor, IL-1beta, and monocyte chemoattractant protein-1 mRNA.
 Furthermore, basal mRNA levels of these cytokines showed strong
 correlation with each other ($p < 0.01$ in all combination) but not with
 tumor necrosis factor-alpha or transforming growth factor-beta1. Plasma
 level of C-reactive protein was highest in the unstable angina
 patients (1.63 ± 0.70 mg/l) and lowest in the control subjects
 (0.22 ± 0.08 mg/l) ($P = 0.03$). We also observed a high correlation
 between C-reactive protein level and the occurrence of minor and major
 coronary events during 6 months of follow-up. Activation status of
 T-cells, assessed by the percentage of HLA-DR positive
 cells, was highest in the unstable angina patients ($26.8 \pm 1.4\%$)
 compared with that in the control ($14.7 \pm 1.2\%$) ($P = 0.0053$). Our data
 represent the first case showing that the circulating monocytes in
 angina patients are activated to a state express numerous
 proatherogenic cytokines. These results may help to diagnose
 angina patients according to the inflammatory markers and evaluate
 the prognosis of the disease.

L13 ANSWER 6 OF 13 MEDLINE on STN
 AN 1999417068 MEDLINE
 DN PubMed ID: 10488965
 TI Plasma levels of interleukin 2, 6, 10 and phenotypic
 characterization of circulating T lymphocytes in
 ischemic heart disease.
 AU Mazzone A; De Servi S; Vezzoli M; Fossati G; Mazzucchelli I; Gritti D;
 Ottini E; Mussini A; Specchia G
 CS Department of Internal Medicine and Therapeutics, University of Pavia,
 IRCCS S. Matteo Hospital, Italy.. a.mazzone@smatteo.pv.it
 SO Atherosclerosis, (1999 Aug) Vol. 145, No. 2, pp. 369-74.
 Journal code: 0242543. ISSN: 0021-9150.
 CY Ireland
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199910
 ED Entered STN: 26 Oct 1999
 Last Updated on STN: 26 Oct 1999
 Entered Medline: 13 Oct 1999
 AB The purpose of this study was to assess lymphocyte receptors expression in
 patients with ischemic heart diseases, as well as to measure the plasma
 levels of interleukin (IL) 2, 6 and 10. T
 Lymphocytes are found in large numbers in human atherosclerotic
 plaques, indicating that immune and inflammatory mechanisms are important
 factors in the pathogenesis of atherosclerosis. Recent data have also

implicated **T lymphocytes** in the pathogenetic mechanism of unstable **angina** and ischemic heart disease. Three groups of patients were studied: 42 with an acute ischemic syndrome (AIS), 36 with stable **angina** (SA) and 39 healthy controls. To characterize lymphocyte phenotype, flow cytometry was performed in whole-blood samples. IL-2, IL-6 and IL-10 were measured using the ELISA method. Double fluorescence evaluation showed an increase in CD8+/CD11b+ cells (cytotoxic **T lymphocytes**) and in CD11b+/CD16+CD56+ cells (NK lymphocytes) in the AIS group and in SA group as compared to the control group ($P < 0.05$ and $P < 0.001$, respectively). IL-2 was increased in the AIS and SA groups compared to the control group (AIS 4.5 ± 0.5 pg/ml; SA 6.3 ± 0.6 pg/ml; controls 2.4 ± 0.8 pg/ml, $P < 0.05$), whereas IL-6 was higher in the AIS group than in the other two groups (AIS 10.8 ± 1.8 pg/ml; SA 1.8 ± 0.8 pg/ml; controls 1.2 ± 0.6 pg/ml, $P < 0.0001$). These data show that patients with ischemic heart disease have an increase in circulating cytotoxic **T lymphocytes** and in IL-2 plasma levels, irrespective of their clinical presentation, compared to normal control subjects, whereas IL-6 is elevated only in patients with AIS.

L13 ANSWER 7 OF 13 MEDLINE on STN
 AN 1999025811 MEDLINE
 DN PubMed ID: 9809939
 TI Immune system activation follows inflammation in unstable **angina** : pathogenetic implications.
 AU Caligiuri G; Liuzzo G; Biasucci L M; Maseri A
 CS Department of Cardiology, Catholic University, Rome, Italy..
 giuseppina.caligiuri@cmm.ki.se
 SO Journal of the American College of Cardiology, (1998 Nov) Vol. 32, No. 5, pp. 1295-304.
 Journal code: 8301365. ISSN: 0735-1097.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199811
 ED Entered STN: 6 Jan 1999
 Last Updated on STN: 6 Jan 1999
 Entered Medline: 20 Nov 1998
 AB OBJECTIVES: The aim of this study was to assess the relations between inflammation, specific immune response and clinical course in unstable **angina** (UA). BACKGROUND: Several studies suggest that either inflammation and/or T-cell activation might have a pathogenetic role in UA, but neither their potential reciprocal connection nor their relation to the clinical course is known. METHODS: Serum levels of C-reactive protein (CRP) (inflammation), IgG, IgA, IgM, C3, C4 (humoral immunity), IL-2 and the percentage of CD4+, CD8+ and CD3+/DR+ T-cells (cell-mediated immunity) were measured in 35 patients with UA and 35 patients with chronic stable **angina** (CSA) during a period of 6 months. RESULTS: The CRP levels and the main specific immune markers (CD4+ and CD3+/DR+ cells, IL-2 and IgM) were higher in unstable than in stable **angina**. In UA, the serum levels of IgM and IL-2 and the percentage of double positive CD3+/DR+ significantly increased at 7 to 15 days, and returned to baseline at 6 months. The increment of circulating activated T cells (CD3+/DR+) in UA was inversely related to the admission levels of CRP ($r = -0.63$, $p = 0.003$) and associated with a better outcome. CONCLUSIONS: Our data suggest that the inflammatory component systemically detectable in UA may be antigen-related and that the magnitude of the immune response correlates with the clinical outcome of instability.

*postulates
elates
provisional*

L13 ANSWER 8 OF 13 MEDLINE on STN
 AN 1998436543 MEDLINE
 DN PubMed ID: 9764052
 TI Recent activation of the plaque immune response in coronary lesions

underlying acute coronary syndromes.

AU van der Wal A C; Piek J J; de Boer O J; Koch K T; Teeling P; van der Loos C M; Becker A E

CS Department of Cardiovascular Pathology, University of Amsterdam, Netherlands.

SO Heart (British Cardiac Society), (1998 Jul) Vol. 80, No. 1, pp. 14-8. Journal code: 9602087. ISSN: 1355-6037.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199810

ED Entered STN: 21 Oct 1998
Last Updated on STN: 21 Oct 1998
Entered Medline: 14 Oct 1998

AB OBJECTIVE: To discriminate between chronic inflammation and acute activation of the plaque immune response in culprit lesions of patients with acute coronary syndromes. DESIGN: Retrospective study. SETTING: Tertiary referral centre. SUBJECTS: 71 patients having coronary atherectomy were classified according to their ischaemic syndrome: stable angina (n = 23); stabilised unstable angina (n = 18); refractory unstable angina (n = 11); and acute myocardial infarction (n = 19). MAIN OUTCOME MEASURES: Immunohistochemical measurement of interleukin 2 receptor (IL-2R) (CD25) positive cells expressed as a percentage of the total amount of (CD3 positive) T lymphocytes in frozen sections of atherectomy specimens. RESULTS: The number of lesions containing IL-2R (CD25) positive T cells increased with severity of the ischaemic coronary syndrome (stable angina, 52%; stabilised unstable angina, 77.8%; refractory unstable angina, 90.9%; acute myocardial infarction, 89.4%). The percentage of activated T cells (CD25/CD3 ratios x100) increased in lesions associated with refractory unstable angina (7.8%) and acute myocardial infarction (18.5%), compared with those in lesions associated with either chronic stable angina (2.2%) or stabilised unstable angina (3.3%). CONCLUSIONS: An increase in the percentage of IL-2R positive T lymphocytes in culprit lesions of patients with acute coronary syndromes indicates recent activation and amplification of the immune response within plaques. This may result in a burst of inflammatory products with tissue degrading and vasoactive properties and, hence, could initiate or accelerate the onset of an acute coronary event.

L13 ANSWER 9 OF 13 MEDLINE on STN

AN 1998090233 MEDLINE

DN PubMed ID: 9430368

TI Systemic inflammatory responses in acute coronary syndrome: increased activity observed in polymorphonuclear leukocytes but not T lymphocytes.

AU Takeshita S; Isshiki T; Ochiai M; Ishikawa T; Nishiyama Y; Fusano T; Toyozumi H; Kondo K; Ono Y; Sato T

CS Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan.. satoshi-t@in.aix.or.jp

SO Atherosclerosis, (1997 Dec) Vol. 135, No. 2, pp. 187-92. Journal code: 0242543. ISSN: 0021-9150.

CY Ireland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199802

ED Entered STN: 17 Feb 1998
Last Updated on STN: 17 Feb 1998
Entered Medline: 5 Feb 1998

AB BACKGROUND: Local inflammation within the coronary arteries is involved in the pathogenesis of acute coronary syndrome. However, the contribution of

a systemic inflammatory response to the pathogenesis of this syndrome has not been well characterized. Accordingly, we investigated systemic inflammatory responses in patients with acute coronary syndrome. METHODS: A total of 83 patients with ischemic heart disease (15 with stable exertional **angina** and 68 with acute coronary syndrome) were studied. The luminol-dependent chemiluminescence (CL) response of polymorphonuclear leukocytes (PMNs), which reflects their ability to generate oxygen species, was used as a marker for PMN activation. Soluble interleukin-2 receptor (sIL-2R) levels were measured to assess T-lymphocyte activation. RESULTS: CL counts of whole blood from patients with acute coronary syndrome were twice those of patients with stable **angina** (2.38 ± 0.22 vs $1.10 \pm 0.17 \times 10^6$ counts, $P < 0.05$). A comparison of CL counts between patients with unstable **angina** and those with acute myocardial infarction revealed no significant differences. T-lymphocyte activity, measured by serum sIL-2R, was significantly lower in patients with acute coronary syndrome than those with stable **angina** (214.3 ± 11.5 vs 358.3 ± 115.7 U/ml, $P < 0.05$). CONCLUSIONS: This investigation shows that there is a systemic increase in PMN activity and a decrease in T-lymphocyte activity in patients with acute coronary syndrome. This contrasts with the pattern of cellular activation seen at sites of local inflammation within atherosclerotic plaques, suggesting that two independent inflammatory processes (local and systemic) may be involved in the pathogenesis of this syndrome.

L13 ANSWER 10 OF 13 MEDLINE on STN

AN 97261213 MEDLINE

DN PubMed ID: 9107167

TI Acute T-cell activation is detectable in unstable **angina**.

AU Neri Sernerri G G; Prisco D; Martini F; Gori A M; Brunelli T; Poggesi L; Rostagno C; Gensini G F; Abbate R

CS Clinica Medica Generale e Cardiologia, Florence, Italy.

SO Circulation, (1997 Apr 1) Vol. 95, No. 7, pp. 1806-12.

Journal code: 0147763. ISSN: 0009-7322.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; AIDS

EM 199705

ED Entered STN: 23 May 1997

Last Updated on STN: 23 May 1997

Entered Medline: 13 May 1997

AB BACKGROUND: Recent studies suggest a role for inflammation in the pathophysiology of unstable **angina**. This study was designed to investigate whether circulating lymphocytes are involved in the inflammatory reaction associated with the episodes of unstable **angina**. METHODS AND RESULTS: Twenty-nine patients with proven unstable **angina**, 36 with stable **angina**, and 30 healthy subjects were studied. Both early and short-lived (interleukin-2 receptor [IL-2R], alpha-chain CD25, and transferrin receptor CD71) and late antigen (HLA-DR) expression were investigated by flow cytometric analysis. Soluble IL-2R (sIL-2R) was also measured in plasma by ELISA. Lymphocyte activation was studied at day 1 of hospital admission and after 7, 15, 30, 60, and 90 days. In patients with unstable **angina**, the number of HLA-DR+ CD3 lymphocytes and levels of sIL-2R were higher ($P < .001$) than in patients with stable **angina** and control subjects. Both CD4+ and CD8+ lymphocytes expressed HLA-DR antigens. No differences were found among the different groups of subjects in regard to the expression of CD25 and CD71. Lymphocyte activation was more marked in patients with urgent revascularization. No relationships were found between the number of HLA-DR+ lymphocytes and either the severity of coronary angiographic lesions or the number of ischemic episodes. Observations over time showed a gradual decrease in the number of HLA-DR+ lymphocytes and sIL-2R levels from weeks 3 through 8 to 12. CONCLUSIONS:

The present results indicate that (1) CD4+ and CD8+ circulating lymphocytes are activated in patients with unstable **angina**, and their activation state lasts 6 to 8 weeks; and (2) activation of lymphocytes is not a consequence of myocardial ischemia. These results support the immune system-mediated inflammatory nature of unstable **angina**.

L13 ANSWER 11 OF 13 MEDLINE on STN
AN 97192236 MEDLINE
DN PubMed ID: 9040055
TI Plasma levels of the monocyte chemotactic and activating factor/monocyte chemoattractant protein-1 are elevated in patients with acute myocardial infarction.
AU Matsumori A; Furukawa Y; Hashimoto T; Yoshida A; Ono K; Shioi T; Okada M; Iwasaki A; Nishio R; Matsushima K; Sasayama S
CS Department of Cardiovascular Medicine, Kyoto University, Sakyo-ku, Japan.
SO Journal of molecular and cellular cardiology, (1997 Jan) Vol. 29, No. 1, pp. 419-23.
Journal code: 0262322. ISSN: 0022-2828.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 9 Jun 1997
Last Updated on STN: 9 Jun 1997
Entered Medline: 27 May 1997
AB Cardiac inflammatory responses appear to play a pivotal role in scar formation after acute myocardial infarction. Monocyte chemotactic and activating factor (MCAF) monocyte chemoattractant protein-1 (MCP-1) is a **cytokine** with chemotactic activity for mononuclear phagocytes, but also for NK cells, T cells, mast cells, and basophils. To investigate the possible involvement of MCAF/MCP-1 in the pathogenesis, its course was studied in patients with acute myocardial infarction. Twenty-three consecutive patients with acute myocardial infarction and 18 patients with **angina pectoris** were studied. **Cytokines** were measured by enzyme-linked immunosorbent assay. Plasma levels of **interleukin** IL-1alpha, IL-1beta, and IL-2 were below the detection limit of our method. IL-6 and **interferon-gamma** were detected in 17.4%, and tumor necrosis factor-alpha in 13.0% of patients with acute myocardial infarction, but the frequency was not statistically significantly different from that in **angina pectoris**. The plasma level of MCAF/MCP-1 in myocardial infarction tended to increase at 3 h after the onset of chest pain (133 +/- 19 pg/ml, P= 0.06) and was significantly elevated at 9 h (143 +/- 20 pg/ml) when compared with that in **angina pectoris** (87 +/- 6 pg/ml, P<0.05). The MCAF/MCP-1 level remained increased during the 24-hours observation period (P<0.01), and maximum level (168 +/- 13 pg/ml) was seen at 24 hour. The level of MCAF/ MCP-1 correlated significantly with the plasma level of another chemokine, IL-8, at 12 h after the onset of chest pain (r=0.51, P<0.05), suggesting that common stimuli mediate the release of both **cytokines** in myocardial infarction. The identification of MCAF/MCP-1 as an inflammatory mediator in acute myocardial infarction suggests that mononuclear phagocytes may play an important role in the early stage of the disease. ✓

L13 ANSWER 12 OF 13 MEDLINE on STN
AN 95103715 MEDLINE
DN PubMed ID: 7805203
TI T lymphocyte activation in stable **angina** pectoris and after percutaneous transluminal coronary angioplasty.
AU Blum A; Sclarovsky S; Shohat B
CS Coronary Care Unit, Beilinson Medical Center, Petah Tiqva, Israel.

SO Circulation, (1995 Jan 1) Vol. 91, No. 1, pp. 20-2.
Journal code: 0147763. ISSN: 0009-7322.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199502

ED Entered STN: 15 Feb 1995
Last Updated on STN: 15 Feb 1995
Entered Medline: 1 Feb 1995

AB BACKGROUND: Inflammatory reactions have an important part in atherosclerosis. Smooth muscle cells, endothelial cells, monocytes, and **T lymphocytes** are actively involved. The purpose of this study was to assess whether **T lymphocytes** are activated in patients with stable **angina pectoris** who are candidates for a percutaneous transluminal coronary angioplasty (PTCA) and the influence of PTCA on this process. METHODS AND RESULTS: Twenty-four patients participated in the study. All were 40- to 60-year-old men, and all but one underwent successful PTCA. Blood samples were taken 1 day before PTCA and 1 week, 1 month, and 2 months after. Two groups of patients were detected: group A, 11 patients who had high levels of soluble **interleukin-2 receptor (sIL-2R)** before PTCA that decreased toward normal during the follow-up period in most of them; and group B, 13 patients who did not have elevated sIL-2R levels before PTCA and in whom sIL-2R levels did not change after the procedure. Group C consisted of 15 healthy men whose sIL-2R levels were in the normal range (control subjects). CONCLUSIONS: (1) **T lymphocytes** are activated in stable **angina** patients. (2) The level of sIL-2R can be a reliable laboratory marker for follow-up of patients after PTCA, especially those with high sIL-2R levels before the procedure. ✓

L13 ANSWER 13 OF 13 MEDLINE on STN

AN 91368708 MEDLINE

DN PubMed ID: 1892066

TI Coronary atherosclerotic plaques with and without thrombus in ischemic heart syndromes: a morphologic, immunohistochemical, and biochemical study.

AU Arbustini E; Grasso M; Diegoli M; Pucci A; Bramerio M; Ardissino D; Angoli L; de Servi S; Bramucci E; Mussini A; +

CS Department of Pathology, Universita di Pavia, Italy.

SO The American journal of cardiology, (1991 Sep 3) Vol. 68, No. 7, pp. 36B-50B.
Journal code: 0207277. ISSN: 0002-9149.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199110

ED Entered STN: 3 Nov 1991
Last Updated on STN: 3 Nov 1991
Entered Medline: 11 Oct 1991

AB We investigated incidence, severity, and distribution of coronary atherosclerosis, acute thrombosis, and plaque fissuring in ischemic heart disease (both unstable-acute syndromes and chronic ischemia) and in nonischemic controls. We also studied the structural, immunohistochemical, and biochemical profile of plaques, with and without thrombus, including morphometry, immunophenotyping of inflammatory infiltrates, **cytokine** presence, and ultrastructural features. Critical coronary stenosis was almost the rule in both acute and chronic ischemic series (greater than 90%) whereas it reached 50% in control subjects. Thrombosis was principally characteristic of unstable-acute ischemic syndromes (unstable **angina**, 32%; acute myocardial infarction, 52%; cardiac sudden death, 26%) but was also found in chronic ischemia (stable **angina**, 12%; ischemic cardiomyopathy, 14%) and in control subjects (4%). Plaque fissuring without thrombus occurred in ✓

low percentages in lipid-rich, severe eccentric plaques in most series. Major differences were found between pultaceous-rich versus fibrous plaques rather than between plaques with or without thrombus. Pultaceous-rich plaques were frequent in sites of critical stenosis, thrombosis, and ulceration. Inflammatory infiltrates, i.e., T cells, macrophages, and a few beta cells, mostly occurred in lipid-rich, plaques unrelated to thrombus. In adventitia, infiltrates were a common finding unrelated to any syndrome. Necrotizing cytokines such as alpha-TNF were immunohistochemically detected in macrophages, smooth muscle, and intimal cells and detected by immunoblotting in 67% of pultaceous-rich plaques, either with or without thrombus. Immune response mediators such as IL-2 were also expressed in analogous plaques but in a minor percentage (50%-40%). Media were extensively damaged in severely diseased vessels with and without thrombus. Ultrastructural study showed that the fibrous cap was either highly cellular or densely fibrillar. Intimal injury with collagen exposure was often associated with platelet adhesion, whereas foamy cell exposure was not. In conclusion, investigated parameters were essentially similar in plaques, both with and without thrombus, whereas major differences were found between pultaceous-rich and fibrous plaques. Since platelets adhere to exposed collagen and not to foam cells, the type of exposed substrates could play a major role in thrombosis.

=> LOG Y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

7.54

7.75

STN INTERNATIONAL LOGOFF AT 12:14:24 ON 24 APR 2006